REMARKS

In an office action dated September 21, 2004, claims 85-88, 91 and 96 have been rejected under 35 U.S.C. §102(b). Claims 90, 92-95 and 97-99 have been objected to. In response, Applicants provide the herein remarks. Claims 85-99 are pending in the application.

The Invention

The invention is directed to peptides that are derived from a protein called "lipopolysaccharide binding protein (LBP)," and modified. The claimed peptides are of restricted length, from 14 to 22 amino acid residues, and have unnatural modifications.

The claimed peptides are identical to SEQ ID NO:1 except that SEQ ID NO:1 has undergone one of the amino acid substitutions defined in (i) through (iv) of claim 85. Also, the modified SEQ ID NO:1 peptide can optionally have an extension of up to 4 amino acid residues at each end of the peptide.

SEQ ID NO: 1 contains 14 amino acid residues, namely, Arg Val Gln Gly Arg Trp Lys Val Arg Lys Ser Phe Phe Lys. This sequence occurs naturally, not as a peptide, but as part of LBP.

The present invention does not claim SEQ ID NO:1, or peptides containing the same. Instead, the present invention claims peptides that differ from SEQ ID NO: 1 by one amino acid substitution, and optionally, by extensions of up to 4 amino acid residues at either end of the sequence.

Applicants have discovered that the claimed substitutions to SEQ ID NO:1 confer vigorous LPS-binding and neutralizing activity to the peptides of the invention.

Rejections Under 35 U.S.C. §102(b)

In the office action, claims 85-88, 91 and 96 have been rejected under §102(b) as being anticipated by U.S. Patent No. 5,731,415 to Gazzano-Santoro et al. (`415 patent).

The `415 Patent

According to the Examiner, the `415 patent teaches a LPS binding protein derived from SEQ ID NO:1, and therefore, anticipates the claimed invention. The Examiner specifically points to column 6, lines 55-65, and column 28, lines 55-65 of the `415 patent as disclosing the claimed substitution modification of SEQ ID NO:1. Applicants respectfully disagree.

Importantly, the derivatives disclosed in the `415 patent lack the carboxy terminal-associated elements characteristic of the LBP holoprotein which enable LBP to bind to and interact with the CD14 receptor on monocytes and macrophages as to provide an immunostimulatory signal to monocytes and macrophages. See column 4, lines 3-9 of the `415 patent.

The interest of the `415 patent is to provide LBP derivatives still having the ability to bind to LPS but no longer having the CD14-mediated immunostimulatory properties of LBP. See column 3, line 67 to column 4, line 3 of the `415 patent.

In the `415 patent, the disclosure of LBP protein derivatives concerns LBP fragments comprising an amino-terminal region of LBP, e.g. amino acid residues 1-197 (See column 4, lines 10-22). LBP derivative hybrid proteins comprise hybrids of LBP protein sequences with the amino acid sequences of other polypeptides, such as fusions of LBP amino-terminal

fragments with polypeptide sequences of other proteins, such as BPU, immunoglobulins and the like. See column 4, lines 23-30 of the `415 patent.

The LBP derivatives and LBP derivative hybrid proteins disclosed in the `415 patent have in common that a part of LBP has been removed (more specifically the carboxy-terminal elements which enable LBP to bind to and to interact with the CD14 receptor on monocytes and macrophages), the remaining part is however authentic (non-modified, native) and (in the hybrids) may be fused to part of a different molecule such as BPI. See column 5, lines 66 up to Example 1, including the passage referred to by the Examiner in column 6, lines 55-65.

With regards to column 6, lines 55-65, this passage describes LBP hybrid proteins comprising a part of LBP into which a part of another LPS binding protein (e.g. BPI) has been inserted or substituted. The term "inserted" means that an amino acid sequence of, e.g. BPI, has been inserted into (i.e. added to) the LBP amino acid sequence. The term "substituted" means that a part of the LBP amino acid sequence has been replaced by an amino acid sequence of, e.g. BPI. As indicated in column 6, lines 62-65 of the `415 patent, the inserted or substituted amino acid sequence from, e.g. BPI, may comprise as few as five continuous amino acids but preferably include ten or more continuous amino acids.

The paragraph starting at column 6, line 66, further clarifies what is meant by "substituted." It mentions that the LBP derivative hybrid proteins in which all or portions of the LPS binding regions of BPI are substituted into the corresponding region of LBP thus include those comprising at least a part of an LPS binding domain of BPI selected from a certain group of amino acid sequences (sequence nos. 17, 18 and 19), each consisting of several tens of amino acid residues.

What is not disclosed or suggested in the `415 patent is a peptide as claimed in the present invention, which comprises amino acid SEQ ID NO. 1 (RVQGRWKVRKSFFK) with one modification therein as defined in claim 85.

With regards to column 28, lines 50-65 (Example 23), said example discloses LBP derivatives in the form of synthetic LBP peptides which comprise portions of the LBP sequence corresponding to either of BPI domain II or III. The LBP derivative designated LBP-1 consists of residues 73 through 99 of LBP having SEQ ID NO: 43. Its sequence (as depicted in column 28, line 57) comprises the sequence RVQGRWKVRKSFFK, which is identical to SEQ ID NO. 1 in the present application. The single modification required in claim 85 is missing. The LBP derivative disclosed in `415 comprises the unmodified native sequence. Thus, the `415 patent does not anticipate the claimed invention.

Therefore, since the `415 patent does not disclose the claimed peptides, it can not be found to anticipate the claimed invention. Accordingly, Applicants respectfully request that the rejection under §102(b) be reconsidered and withdrawn.

In light of the above discussion, Applicants respectfully request that the Examiner reconsider the rejection under 102(b) based on the `415 patent.

Arana et al.

Claim 85 has been rejected under §102(b) as being anticipated by Arana et al. (*Biotecnologia Aplicada*, Vol. 12, No. 2, 1995). The examiner contends that Arana et al. disclose peptides derived from a protein called LBP. See p. 101. He further states that Arana et al. teach a 14 amino acid residue peptide identical to SEQ ID NO. 1 having undergone one amino acid modification. Applicants disagree.

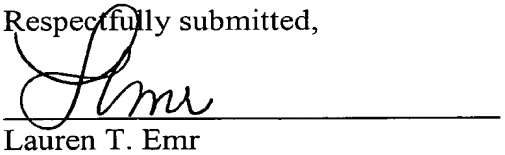
There is not the slightest hint in Arana et al. to modify SEQ ID NO 1 as in claim 85. Arana et al. do not teach a peptide as claimed in present claim 85 which comprises a sequence differing from SEQ ID NO. 1 by one amino acid substitution as defined in said claim 85.

Perhaps the Examiner has been mislead by the random mutagenesis experiments mentioned in the last sentence of the introduction and illustrated in the second half of the results and discussion section of Arana et al. It is noted that the random mutagenesis disclosed by Arana et al. concerns human interleukin-2 (hiL-2) and not peptides derived from LBP or other LPS-binding proteins.

Accordingly, since Arana et al. do not disclose the claimed peptides, it is respectfully requested that the Examiner reconsider and withdraw the rejection under §102(b) based on Arana et al.

In light of the foregoing remarks, Applicants respectfully submit that the application is now in condition for allowance. If Examiner Shannon-Shah believes a telephone discussion with the Applicants' representative would be of assistance, he is invited to contact the undersigned at his convenience.

Respectfully submitted,



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